

LETTER TO THE EDITOR

Reflections and Proposals for the Worldwide Standardization of Lymphadenectomy for Gastric Carcinoma

Dear Sir,

In 1999, well-recognized and clearly defined procedures for lymphadenectomy in gastric cancer are lacking and this shortfall is highly detrimental. Procedures need to be standardized with practical guidelines for physicians and be easy to perform so that they are reproducible everywhere. Results should be presented clearly, simply, and be highly informative with a uniform terminology to be used worldwide when publishing and comparing treatment results.

The UICC TNM classifications [1–3] only offer recommendations for the formulation of histologic results. The guidelines and classification of the Japanese Research Society for Gastric Cancer [4] are well defined but are complex and virtually impossible to reproduce in routine practice [5], even if they were very useful research tools. They are based on the anatomic extent of lymph node (LN) metastases, stations changing according to the location of the tumor in the stomach. An excellent quality control study was conducted by Dutch surgeons during a prospective multicentric randomized study comparing Japanese D2 vs. D1 lymphadenectomies [5]. In spite of the presence of one of the eight expert surgeons during all the D2 lymphadenectomies, *non-compliance* (i.e., no yield of LN from indicated stations according to the randomization) occurred in 84% of the cases and *contamination* (i.e., one or more LN found in stations for which dissection was not indicated) occurred in 48% and 52% of cases for D1 and D2 lymphadenectomies, respectively. Surgeons and pathologists were considered to have contributed equally to non-compliance [5]. This study clearly demonstrates that the Japanese procedure is not routinely feasible, as verified during the daily practice of each and everyone of us, and this is also the case for Japanese surgeons themselves (the Japanese surgeon who participated in the Dutch study had a personal score of 43% for non-compliance). Therefore, it cannot be considered a standardized reproducible guideline to be applied worldwide. Moreover, in practice, the only foolproof way to localize the 16 different groups of LN described in the Japanese guideline

is to separate them, one by one, during the lymphadenectomy. This implies numerous sections of lymphatic and vascular vessels during surgery and thus an increased risk of regional seeding of tumor cells [6]. The only safe technique is the en bloc lymphadenectomy, which, once complete, prohibits subsequent unequivocal distinction of each group of LN.

The number of LN that should be resected during lymphadenectomies is important. The greater the number of LN analyzed, the greater the probability of finding positive LN [3]. Simply analyzing a small number LN considerably increases the risk of understaging patients. After a thorough examination of the works of the German Gastric Cancer Study Group and of the Erlangen Group [7], the UICC 1997 classification recommended the examination of at least 15 LN for a lymphadenectomy, whatever the type, for gastric carcinoma [2]. This means that at least 15 LN must be negative for a patient to be staged confidently as No. A quality control analysis should be envisaged everywhere to certify that this minimal number of LN has been studied. This also signifies that a D1-type lymphadenectomy must resect at least 15 LN. In addition, it would be of interest to establish a minimal number of LN for the D2-type lymphadenectomy. Mean numbers of LN have been reported by different teams (Table I) and 25 LN clearly appear to be the usual lower limit for a D2-type lymphadenectomy. Recently, it has been proved that Japanese LN staging based on the anatomic extent of the invaded LN yields less prognostic information than the new 1997 UICC LN staging system based on the number of invaded LN [7,13]. This LN status, based simply on the number of invaded LN, thus appears to be the best way to present the results of the surgical and histological procedures, with four groups (No when 0 LN are invaded, N1 when

*Correspondence to: Dominique Elias, MD, Departement de Chirurgie Oncologique, Rue Camille Desmoulins, 94805, Villejuif Cedex, France. Fax No.: (33) 01 42 11 52 56. E-mail: elias@igr.fr

Accepted 12 March 1999

TABLE I. Analysis of the Number of Resected LN According to the Type of Lymphadenectomy*

Author	No. of patients	Mean No. of studied LN		
		D1	D2	D3
Siewert et al. [8]	1,654	15	35.4	42.6
Soga et al. [9]	530	—	30	—
Ichikura et al. [10]	777	—	33	—
de Manzoni et al. [11]	162	18	31	47
Bonenkamp et al. [12]	996	18.4	31.5	—

*The types of lymphadenectomy (D1, D2, and D3) are defined according to the Japanese classification [4].

1–6 LN are invaded, N2 when 7–15 LN are invaded, and N3 when more than 15 LN are invaded).

We elaborate proposals for standardized, simple, reproducible lymphadenectomies for gastric cancers taking these facts into consideration. They are based on: 1) three LN dissection planes (indicating simply the type of lymphadenectomy performed); 2) the location of the tumor in the stomach is not taken into account (except in two specific cases); and 3) results are given according to the 1997 UICC staging system. Most infiltrating gastric carcinomas will be treated with the following simple lymphadenectomy removing the LN at anterior plane I around the great and small curves of the stomach (i.e., Japanese LN stations 1–6) and the LN at intermediate plane II along the three gastric arteries (i.e., Japanese LN stations 7–9). The first centimeters of the LN along the splenic artery (station 11) are then removed without performing a splenectomy (station 10) or a caudal pancreatectomy, which, in most cases, do not offer any therapeutic benefit [14,15] and which considerably increase postoperative morbidity and mortality [12,16]. Thus, LN at posterior plane III (beside the aorta and vena cava) are not resected in this standardized surgical approach.

Two particular tumor sites should not be treated with this standard resection of planes I and II: 1) When the tumor is located in the antrum, a subtotal gastrectomy is recommended because a French randomized study comparing total and subtotal gastrectomy showed that 5-year survival rates were similar but that the functional status was better with subtotal gastrectomy [17]. Subtotal gastrectomy almost completely resects the small curve of the stomach (and, of course, the left gastric artery), which then facilitates resection of the right esophageal LN, but not the left esophageal LN, which is left in place. The small, remaining upper part of the stomach is vascularized by the small vessels of the upper part of the great curvature. 2) When the tumor is located in the upper part of the great curvature and is also invading the serosa, a splenectomy is appropriate with a meticulous splenic lymphadenectomy, because these LN are invaded in 25–30% of cases [18].

It is highly probable that this standard procedure,

which is close to the Japanese D2 lymphadenectomy, will procure more therapeutic effects than a more limited lymphadenectomy. The negative Dutch randomized study [19] comparing D1 and D2 lymphadenectomies was highly informative for it provided a whole body of data on the non-reproducibility of Japanese lymphadenectomies and underlined the fact that mortality and morbidity were on the increase due to splenopancreatectomy [12,19]. Operative mortality was 10% for D2 lymphadenectomy vs. 4% for D1 lymphadenectomy ($P = 0.004$), with 43% of complications for D2 vs. 25% for D1 lymphadenectomy ($P < 0.001$) [19]. In contrast, the recent results of D2 lymphadenectomy with pancreas preservation reported by the Italian Gastric Cancer Study Group were well below these rates, with only 3.1% for mortality and 20.9% for morbidity [20]. A further multicenter randomized study comparing the two simplified and reproducible plane I and plane II lymphadenectomies without splenopancreatectomy is necessary so that definitive conclusions can be drawn.

In conclusion, these simple, reproducible rules for lymphadenectomy and histological analysis should offer a basis permitting discussion and eventually may lead to the standardization of the procedures worldwide.

ACKNOWLEDGMENTS

The author gratefully acknowledges Lorna Saint-Ange for editing the manuscript.

Dominique Elias, MD*

Department of Surgical Oncology
Institut Gustave Roussy
Comprehensive Cancer Center
Villejuif, France

REFERENCES

1. Hermanek P, Sobin LH (eds): "TNM Classification of Malignant Tumours. International Union Against Cancer." 4th Edition, 2nd Revision. Berlin: Springer, 1992.
2. Sobin LH, Wittekind CH (eds): "TNM Classification of Malignant Tumours. International Union Against Cancer." 5th Edition. New York: John Wiley & Sons, 1997.
3. Hermanek P, Henson DE, Hutter RV, et al. (eds): "TNM Supplement, 1993: A Commentary on Uniform Use. International Union Against Cancer." Berlin: Springer, 1993.
4. Nishi M, Omori Y, Miwa K (eds): "Japanese Classification of Gastric Carcinoma. Japanese Research Society for Gastric Cancer (JRS GC)." 1st English Edition. Tokyo: Kanehara and Co., 1995.
5. Bunt AM, Hermans J, Boon MC, et al.: Evaluation of the extent of lymphadenectomy in a randomized trial of Western- versus Japanese-type surgery in gastric cancer. *J Clin Oncol* 1994;12: 417–422.
6. Jacquet P, Elias D, Sugarbaker PH: L'implantation tumorale dans les sites de cicatrisation après chirurgie des cancers digestifs. *J Chir (Paris)* 1996;133:175–182.
7. Roder JD, Bottcher K, Busch R, et al.: Classification of regional lymph node metastasis from gastric carcinoma. *Cancer* 1998;82: 621–631.
8. Siewert JR, Bottcher K, Roder JD, et al.: Prognostic relevance of systematic lymph node dissection in gastric carcinoma. *Br J Surg* 1993;80:1015–1018.

9. Soga J, Ohayama S, Miyashita K, et al.: A statistical evaluation of advancement in gastric cancer surgery with special reference to the significance of lymphadenectomy for cure. *World J Surg* 1988;12:398–405.
10. Ichikura T, Tomimatsu S, Okusa Y, et al.: Comparison of the prognostic significance between the number of metastatic lymph nodes and nodal stage based on their location in patients with gastric cancer. *J Clin Oncol* 1993;11:1894–1900.
11. de Manzoni G, Verlato G, Gugliemi A, et al.: Prognostic significance of lymph node dissection in gastric cancer. *Br J Surg* 1996; 83:1604–1607.
12. Bonenkamp JJ, Songun I, Hermans J, et al.: Randomized comparison of morbidity after D1 and D2 dissection for gastric cancer in 996 Dutch patients. *Lancet* 1995;345:745–748.
13. Kodera Y, Yamamura Y, Shimizu Y, et al.: The number of metastatic lymph nodes: A promising prognostic determinant for gastric carcinoma in the latest edition of the TNM classification. *J Am Coll Surg* 1998;187:597–603.
14. Shiu MH, Perroti M, Brennan MF: Adenocarcinoma of the stomach: A multivariate analysis of clinical, pathologic and treatment factors. *Hepatogastroenterology* 1989;36:7–12.
15. Koga S, Kaibara N, Kimura O, et al.: Prognostic significance of combined splenectomy or pancreaticosplenectomy in total and proximal gastrectomy for gastric cancer. *Am J Surg* 1981;142: 546–550.
16. Cuschieri A, Fayers P, Fielding J, et al.: Postoperative morbidity and mortality after D1 and D2 resections for gastric cancer: Preliminary results of the MRC randomized controlled surgical trial. *Lancet* 1996;347:995–999.
17. Gouzi JL, Huguier M, Fagniez PL, et al.: Total versus subtotal gastrectomy for adenocarcinoma of the gastric antrum. A French prospective controlled study. *Ann Surg* 1989;209:162–166.
18. Noguchi Y, Imada T, Matsumoto A, et al.: Radical surgery for gastric cancer, a review of the Japanese experience. *Cancer* 1989; 64:2053–2062.
19. van de Velde, Dutch Gastric Cancer Study Group: Lymph node dissection in gastric cancer: 5-year results of a randomized trial of D1 and D2 dissection in 996 Dutch patients. *Proc Am Soc Oncol* 1997;16(Abtract 987).
20. Deguili M, Sasako M, Ponti A, et al.: Morbidity and mortality after D2 gastrectomy for gastric cancer: Results of the Italian Gastric Cancer Study Group. Prospective multicenter surgical study. *Clin Oncol* 1998;16:1490–1493.